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Papageorgiou, Spyridon N

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STATISTICAL CORNER

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Spyridon N. Papageorgiou

Clinic of Orthodontics and Pediatric Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland

ORCID Spyridon N. Papageorgiou http://orcid.org/0000-0003-1968-3326

CONTACT Spyridon N. Papageorgiou Clinic of Orthodontics and Pediatric Dentistry, Center of Dental Medicine, University of Zurich, Plattenstrasse 11, Zurich CH 8032, Switzerland; snpapage@gmail.com.

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MANUSCRIPT

Theoretical scenario

Clinical trials using categorical outcomes often express their results as risk, which is the probability with which a health outcome (usually an adverse event) will occur. For this article two scenarios on early treatment of either Class II or Class III malocclusion are discussed.

In the first scenario three widely known randomized trials on early Class II (2-phase) treatment versus delayed (1-phase) treatment are summarized by a recently updated Cochrane review (Batista et al. 2018). For this article, the results of two kinds of early treatment (headgear and functional appliances) have been combined into a single group. Setting other trial results aside, the authors followed patients from the start of early treatment (if administered) to the end of fixed appliance treatment and measured the incidence of new dental trauma. The effect of treatment on new trauma risk (=incidence) is here presented as Relative Risk (RR) with its 95% Confidence Interval (CI). The RR is the appropriate effect size to express a treatment-induced relative change of risk (Sinclair and Bracken 1994).

In the second scenario a long-term randomized trial of early maxillary protraction for Class III treatment compared to no treatment (observation) is presented (Mandall et al. 2016). The authors followed patients from the start of early treatment (if administered) and assessed at 15 years of age their need for orthognathic surgery through a blinded panel of consultants. The effect of treatment on the need for orthognathic surgery is likewise presented as RR with its 95% CI.

The RRs of treatment-induced effects on dental trauma and need for surgery are given in Table 1 with the corresponding 95% CIs.

Table 1 around here (on the first page).

Which of the following statements are correct, if any:

(a) The relative effect size of treatment is similar in the two scenarios.

(b) The absolute effect size of treatment is similar in the two scenarios.

(c) The risk for dental trauma and the need for surgery among treated Class II / Class III patients is similar.

(d) The absolute gains from early Class II or Class III treatment are the same for all patients that are treated early.

Discussion

The first statement refers to the magnitude of the relative effect size, which is here the RR. The two scenarios have similar RRs (both around 0.6) and with similar uncertainty around them (95% CIs of 0.4-0.9 and 0.3-0.9). The p values are somewhat different, but this can be attributed to different sample sizes in the two scenarios and p values do not give information about the magnitude of an effect anyway. Overall, statement (a) is correct.

The second statement refers to the *absolute* effect size, which is different to the *relative* effect size. It is recommended that clinical trials report both relative and absolute effects to give a complete picture of the treatment effects and their implications (Moher et al. 2010). The recommended absolute effect size is the risk difference, which is simply the difference of the two groups' risks. If risk differences are calculated, it is obvious that the absolute effect sizes for the two scenarios differ: -11.4% for the first scenario and -29.3% for the second scenario (Table 2) and therefore, statement (b) is false.

Table 2 around here (on the second or third page).

Even though the relative effects are similar, the absolute effects vary considerably. This has to do with the fact that the patient's baseline (pre-treatment) risk has a direct effect on the absolute gains attained by treatment. This is illustrated in Figures 1 and 2. We see that the baseline risk for dental trauma among untreated Class II patients (in these trials) is 29.1%, while the baseline need for orthognathic surgery among untreated Class III patients (in this trial) is 65.6% (Figure 1 and Figure 2, respectively). Subsequently, early Class II treatment 'saves' 11 of every 100 patients from a dental trauma they would have had if left untreated, while early Class III treatment 'saves' 30 of every 100 patients from orthognathic surgery that would be needed if left untreated. In the end and with the same relative effects, the risks (for trauma/surgery) are reduced in both scenarios compared to untreated patients, but both the absolute risk reduction and the risk of treated patients is different between the two scenarios. So statement (c) is wrong.

Finally, for a given relative effect the absolute risk reduction is directly linked to the patient's baseline risk. In the first scenario about Class II early treatment, this pertains to a patient's baseline risk for dental trauma. It is known however, that not trauma risk is not uniform across the general population and several factors are linked to increased trauma risks, including among others patient sex, obesity, inadequate lip coverage, increased overjet, and involvement into sport activities (Soriano et al. 2007; Glendor 2009). It is reasonable to assume that a normal-weight girl with moderate overjet and adequate lip coverage, who does ballet will have a lower risk for dental trauma than an obese boy with large overjet and inadequate lip coverage, who plays basketball. As can be seen in Figure 3, the expected absolute treatment gains for early Class II correction are different for the hypothetical low-risk girl and high-risk boy. Therefore, statement (d) is false, and the expected net gains of treatment rely on the patients one selects to treat.

References

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TABLES

Table 1. Results of the two clinical scenarios.

Scenario	Outcome	RR	95% CI	P
Early Class II Tx	New dental trauma	0.61	0.42 to 0.87	0.006
Early Class III Tx	Need for orthognathic surgery	0.55	0.33 to 0.93	0.03

CI, confidence interval; RR, relative risk; Tx, treatment.

Table 2. Results of the two clinical scenarios including relative and absolute effects.

Scenario	Outcome	Risk Control	Risk Tx	Effect	95% CI	P
Early Class II Tx	New dental trauma	29.1%	17.7%	RR=0.61	0.42 to 0.87	0.006
				RD=-11.4%	-21.4 to -1.3%	0.03
Early Class III Tx	Need for orthognathic surgery	65.6%	36.3%	RR=0.55	0.33 to 0.93	0.03
				RD=-29.3%	-52.5 to -6.0%	0.01

CI, confidence interval; RD, relative difference; RR, relative risk; Tx, treatment.

Figure 1. Illustrative risks of dental trauma for the scenario of early Class II treatment.

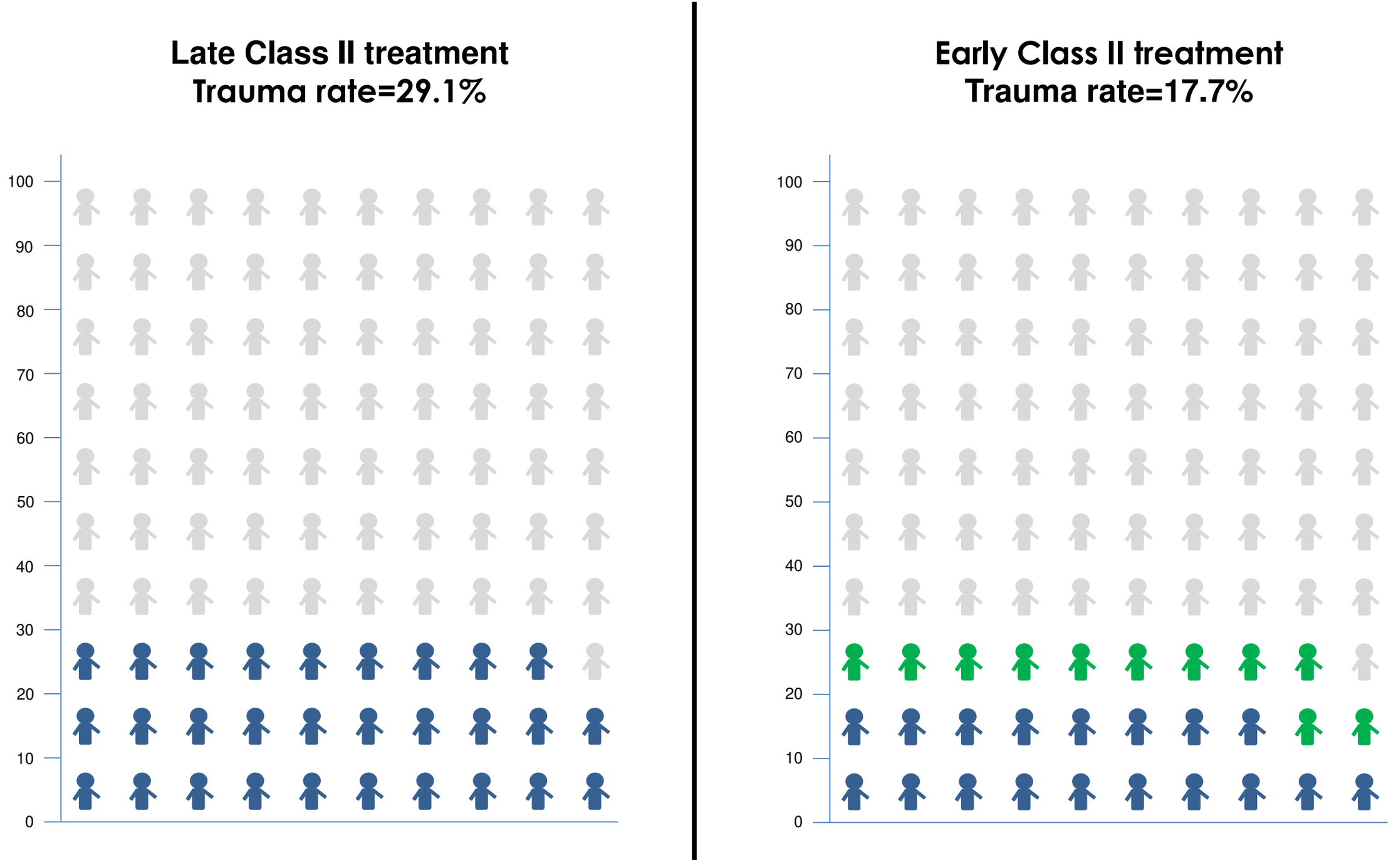

Figure 2. Illustrative risks of need for surgery for the scenario of early Class III treatment

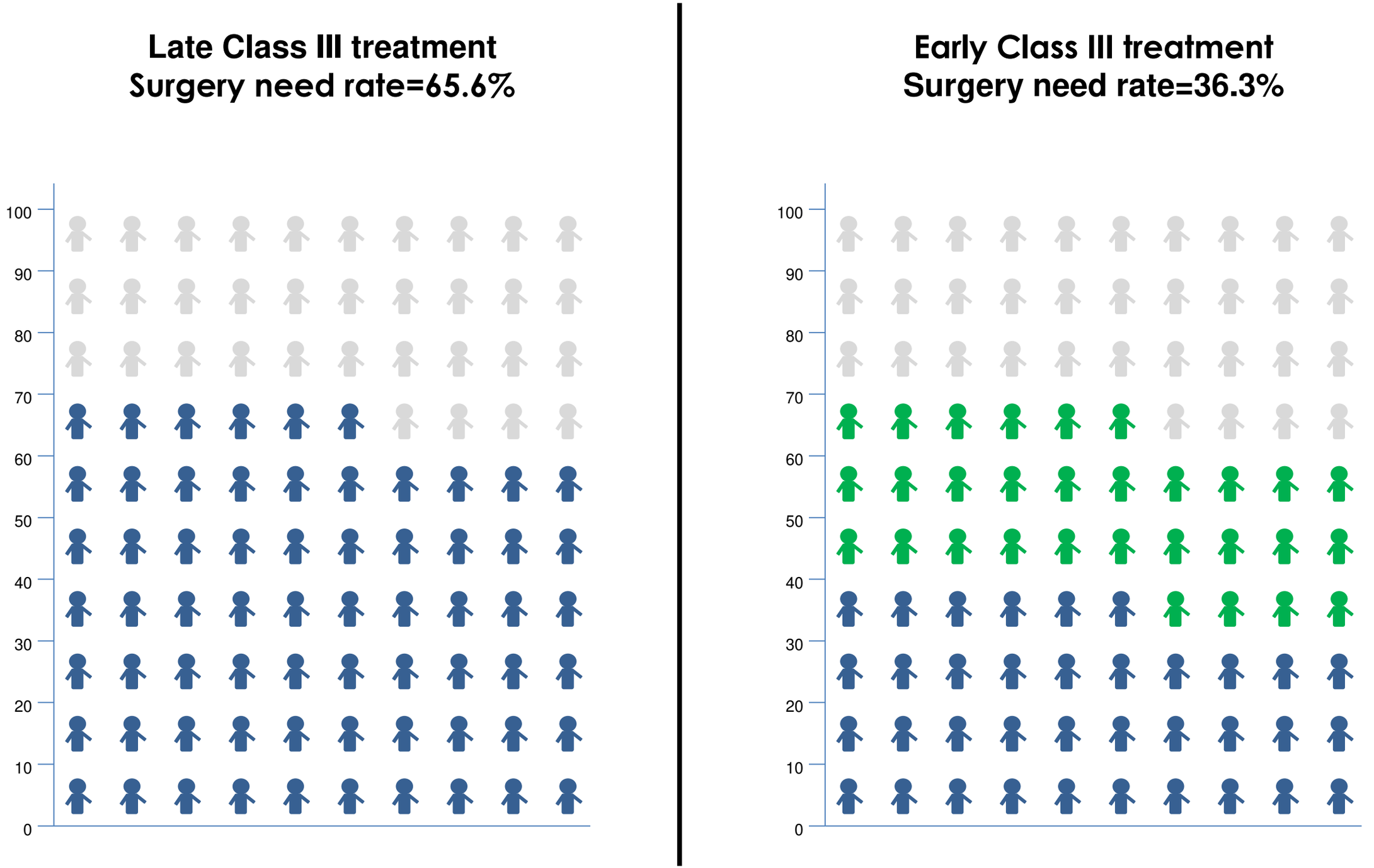

Figure 3. Illustrative gains in terms of dental trauma risk reduction for the scenario of early Class II treatment. Comparison between patients with baseline low risk of trauma and patients with high risk of trauma (assuming a modest high-risk/low-risk ratio of 3).